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EDITORIAL

In this issue...

Laura Erker and **Markus Grompe** provide the review **Signaling networks in hepatic oval cell activation.** Oval cells, also referred to as adult liver stem cells, proliferate and differentiate during liver regeneration. This review explores the factors involved in oval cell activation, proliferation, migration, and differentiation.

In his piece **On the road to reprogramming, Martin Pera** examines the contributions of some recent papers to the rapidly advancing field of iPS cell biology. Included in this analysis is the study published in this issue of *Stem Cell Research* from **Hideki Masaki** and colleagues, **Heterogeneity of pluripotent marker gene expression in colonies generated in human iPS cell induction culture.** Their study identified a marked heterogeneity in morphology and gene expression amongst colonies generated by a four-gene (Oct3/4, Sox2, c-Myc, and Klf4) transduction protocol in human neonatal skin-derived cells. As Martin Pera commented, there was clear evidence for partial reprogramming in many colonies, with only a small minority of colonies displaying an ES cell-like morphology and expressing all eight pluripotency-associated genes examined (chosen on the basis of their consistent expression in human ES cells). Importantly, even colonies retaining a fibroblast-like morphology expressed nanog, TDGF1, and DNMT3b, indicating that the expression of these core pluripotency genes was insufficient to guarantee complete reprogramming. The iPS cell lines that Masaki et al. derived in this study maintained a diploid karyotype, and genome-wide SNP analysis did not reveal any submicroscopic genetic changes in the reprogrammed lines. Pera comments further that these findings provide convincing evidence that genetic alteration is not required for establishment or progressive growth of human iPS cell lines, even in chemically defined media.

The molecular mechanisms controlling DNA-damage-induced apoptosis of human embryonic stem cells (hESC) are poorly understood. The article by **Catarina Grandela** and colleagues, **p53 is required for etoposide-induced apoptosis of human embryonic stem cells,** explores the mechanisms for etoposide induced apoptosis of hESCs. Their study demonstrates that p53 is required for etoposide-induced apoptosis of hESC and that undifferentiated hESC that express Oct4 are much more sensitive to etoposide-induced apoptosis than their more differentiated progeny.

Hematopoietic cells have been demonstrated to survive in many nonhematopoietic tissues after transplantation. Apparent "bone-marrow-derived" cerebellar Purkinje cells in fact result from fusion events and it has been suggested that fusion may be a natural physiological phenomenon to rescue dysfunctioning cells. In their article **Cerebellar heterokaryon formation increases with age and after irradiation, Anita Wiersema** and colleagues show that fusion of transplanted bone marrow cells with resident Purkinje cells is age-dependent and is strongly enhanced when Purkinje cells are damaged by high-dose irradiation.

In their thought-provoking article **Reduction of myocardial infarct size by human mesenchymal stem cell conditioned medium, Leo Timmers** and colleagues demonstrate cardioprotection in a porcine model of ischemia and reperfusion injury by intravenous and intracoronary administration of human MSC secretions. Human MSC-conditioned medium (CM) treatment was associated with a 60% reduction in infarct size and marked improvement of systolic and diastolic cardiac performance. Fractionation studies revealed that the responsible paracrine factor of human MSCs is likely to be a large complex rather than a single small molecule. This study identifies human MSC-CM as a promising therapeutic option for reducing myocardial infarct size in patients with acute MI and suggests a broader therapeutic potential for stem cell secretions.

Still on a cardiac theme, **Marie-José Goumans** and colleagues describe the efficient isolation and propagation of human cardiomyocyte progenitor cells (hCMPCs) from fetal heart and patient biopsies in their paper **TGF-β1 induces efficient differentiation of human cardiomyocyte progenitor cells into functional cardiomyocytes in vitro.** The hCMPC cultures they established from over 70% of adult atrial biopsies differentiated into spontaneously beating myocytes following addition of transforming growth factor β. These are the first cells isolated from human heart that proliferate and form functional cardiomyocytes without requiring co-culture with neonatal myocytes.

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